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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,881	03/28/2002	Akira Matsumoto	082371-000000US	1327

7590

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EXAMINER

SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
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1652

12

DATE MAILED: 01/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/980,881

Applicant(s)

MATSUMOTO, AKIRA

Examiner

Sheridan L. Swope

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 16 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-35 is/are pending in the application.
- 4a) Of the above claim(s) 8,12-17,21-23,27-31 and 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 2-7,9,11,18-20,24-26,32,34 and 35 is/are rejected.
- 7) ☒ Claim(s) 10 and 32 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 March 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Applicant's amendment of Claims 2, 8, 9, 10, 11, 12, 16, and 26 as well as addition of Claims 32-35 in Paper No. 11 is acknowledged.

Applicant's election with traverse of Invention I, Claims 2, 9, 18, 19, 20, and 24-26 in Paper No. 11 is acknowledged. The original restriction was based on the fact that the technical feature linking Groups I-VIII appeared to be that they all relate to proteases that act on brain APP and that Eaton et al, 1991 teach the sequence of a carboxypeptidase which has 98% identity with SEQ ID NO: 2. The traversal is on the grounds that the 98% sequence identity is based on comparison of EMBL Acc# AB011969 with SEQ ID NO: 2. Since the sequence of AB011969 was not available to the public until February 2, 2000 and the claimed priority date of this application is April 30, 1999, applicants argue that the sequence of AB011969 does not constitute prior art. The examiner acknowledges this argument and the restriction based on the sequence of AB011969 is withdrawn.

Unity of Invention

Rule 37 §1.475 describes the basis for Unity of Invention: An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. An international or national stage application containing claims to different categories of inventions will be considered to have unity of invention if, the claims are drawn to a product, a process specially adapted for the manufacture of the said product, and a use of said product.

The inventions listed as Groups I, II, and IV relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they comprise the same or corresponding special technical feature. The special technical feature linking Groups I, II, and IV, is a nucleotide product encoding a protein comprising peptidase activity towards brain APP, said encoded protein, a method of making said protein, and a method of using said protein.

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Accordingly, Groups I, II, and IV are so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

Groups III and V-VIII lack the same special technical feature as the invention of Groups I, II, and IV because they recite products that do not share a special common structural or functional feature with said nucleotides or said proteins of Groups I and II, respectively, or recite methods that do not use the same reagents or produce the same results as the methods of Groups I and IV. Accordingly, Groups III and V-VIII are not so linked to Groups I, II, and IV by the same or a corresponding special technical feature as to form a single general inventive concept with Groups I, II, and IV.

Of the newly added claims, Claims 32, 34, and 35 are restricted into Group I while, Claim 33 is restricted into Group III. Claims 2-7, 9-11, 18-20, 24-26, 32, 34, and 35 are hereby examined.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification-Objections

Specification is objected to for not describing the identity or function of the protein set forth by SEQ ID NO: 4 and its relationship to the proteins set forth by SEQ ID NO: 2 and 3. Clarification is required.

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The specification is further objected to for not stating the identity of the human brain carboxypeptidase used in Example 7. Is this protein the 40kDa or 30kDa protein? Is it a recombinant protein or is it a purified protein from brain? Clarification is required.

Claims-Objections

Claim 32 is objected for lacking an article between “comprises” and “C-terminal”. Either “a” or “the” is needed. Correction is requested.

Claim 10 is objected for lacking “encoding the” between “A polynucleotide” and “C-terminal”. Correction is requested.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3, 5, 6, 7, 9, 11, 18-20, 24-26, and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2, 3, 9, and 32 are indefinite in the recitation of “hybridizes with” as this term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids that will hybridize under some hybridization conditions, will not necessarily hybridize under different conditions. The hybridization conditions described on pages page 11, line 4 to page 12, line 22 are only exemplary and do not define the conditions recited in Claims 2, 3, 9, and 32. Thus, Claims 2, 3, 9, and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Since, Claims 5, 6, 7, 11, 18-20, and 24-26 are dependent on Claim 2 and recite vectors, host cells, methods for producing the protein, methods for screening compounds that bind to the protein, and

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compositions, drugs, and kits comprising the protein of Claim 2, said claims are also rejected for the reasons described for Claim 2.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-7, 11, 18-20, 24-26, 32, 34, and 35 are rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for polynucleotides encoding proteins having peptidase activity towards brain APP and said encoded proteins wherein, said nucleotide is set forth by SEQ ID NO: 1 and said proteins are set forth by SEQ ID NO: 2, SEQ ID NO: 3, or a protein having $\geq 90\%$ identity with by SEQ ID NO: 2 or SEQ ID NO: 3. However, the specification does not reasonably provide enablement for any polynucleotide encoding a protein having peptidase activity towards brain APP wherein said protein is set forth by SEQ ID NO: 4 or has $\geq 90\%$ identity with SEQ ID NO: 4. The specification also does not reasonably provide enablement for any protein having peptidase activity towards brain APP wherein said protein is set forth by SEQ ID NO: 4 or has $\geq 90\%$ identity with SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 2 is so broad as to encompass any protein with protease activity towards APP wherein the protein is set forth by SEQ ID NO: 4 or has $\geq 90\%$ identity with SEQ ID NO: 4. Claim 3 is so broad as to encompass any polynucleotide encoding any protein with protease activity towards APP wherein the protein is set forth by SEQ ID NO: 4 or has $\geq 90\%$ identity

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with SEQ ID NO: 4. Claim 32 is so broad as to encompass the proteins of Claim 2 wherein the protein comprises the C-terminal 14 amino acids of Ser-Asn-Pro-Pro-Val-Glu-Lys-Leu-Leu-Pro-Leu-Ser-Leu-Lys. Claim 35 is so broad as to encompass any protein with protease activity towards APP wherein the protein is set forth by SEQ ID NO: 4 or any variant thereof in which no more than 30 amino acids are replaced, deleted, inserted, and/or added. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides and proteins broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which proteins can be used to obtain the desired protease activity towards APP requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO 2 and SEQ ID NO: 3 and the polynucleotide sequence of SEQ ID NO: 1.

The specification does not support the broad scope of the Claim 2 which encompasses any protein with protease activity towards APP wherein the protein is set forth by SEQ ID NO: 4 or has $\geq 90\%$ identity with SEQ ID NO: 4. The specification does not support the broad scope of the Claim 3 which encompasses any polynucleotide encoding any protein with protease activity towards APP wherein the protein is set forth by SEQ ID NO: 4 or has $\geq 90\%$ identity with SEQ ID NO: 4. The specification does not support the broad scope of the Claim 35 which encompasses any protein with protease activity towards APP wherein the protein is set forth by SEQ ID NO: 4 or any variant thereof in which no more than 30 amino acids are replaced,

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deleted, inserted, and/or added. The specification does not support the broad scope of Claim 2, 3, 32, and 35 because the specification does not establish the identity of SEQ ID NO: 4 and whether the protein set forth by SEQ ID NO: 4 or variants having $\geq 90\%$ identity with SEQ ID NO: 4 have protease activity towards APP.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polynucleotides encoding any number of proteins, as set forth by SEQ ID NO: 4 or having $>90\%$ identity with SEQ ID NO: 4, wherein said proteins have protease activity towards APP. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences derived from SEQ ID NO: 4 having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 2-7, 11, 18-20, 24-26, and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of polynucleotides encoding proteins having protease activity towards APP and said proteins. The specification teaches the structure and function of only two representative species of such polynucleotides and proteins. Moreover, the specification fails to describe the function of the protein set forth by SEQ ID NO: 4 or proteins

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having $\geq 90\%$ identity with SEQ ID NO: 4. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 4-7, 11, 18-20 and 24-26, and 32 are also rejected under 35 U.S.C. 112 first paragraph. Claim 4 recites the DNA of Claim 3 comprising the coding region of SEQ ID NO: 1. Claims 5-7 recite a vector comprising the DNA of Claim 3, a host cell comprising said vector, and a method of making the encoded protein, respectively. Claim 11 recites a method of using the protein of Claim 2. Claims 18-20 recite compositions or drugs comprising the proteins recited by Claim 2. Claims 24-26 recite kits comprising the proteins recited by Claim 2. Claim 32 recites the proteins of Claim 2 comprising the C-terminal 14 amino acids of Ser-Asn-Pro-Pro-Val-Glu-Lys-Leu-Leu-Pro-Leu-Ser-Leu-Lys. Therefore, Claims 4-7, 11, 18-20 and 24-26, and 32 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

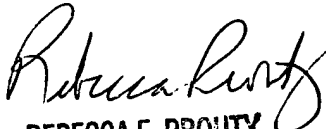
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.


REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1652
1652